Modeling approach to stimulate the formation of Oxidation LDL after intake of different types of fatty acids

By

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Abstract

Oxidized lipoprotein (Ox-LDL) has been studied for over 30 years. Multiple lines of evidence have confirmed that oxidation LDL involved in the development of atherosclerosis. Many mechanisms have been proposed for LDL oxidation. However, the physiologically relevant mechanisms of LDL oxidation are still imperfectly understood.

The component of VLDL, mainly consist of cholesterol and triglyceride, sometimes has unsaturated fatty acids tail. We assume that the free radical can react with these unsaturated fatty acids. In this way, the structure of apolipoproteins in LDL will be modified. LDL can be converted to a form that could not be recognized specifically by LDL receptor, but with high affinity to macrophage scavenger receptors, leading to the formation of atherosclerosis.

Based on our assumption, we build a mathematic model to stimulate the process of LDL oxidation. The model demonstrates how different dietary and ratio of unsaturated fatty acids may affect the possibility that LDL convert to oxidation LDL, provide a way to look at LDL oxidation qualitatively and quantitatively.

The goal of this research is to obtain insight into LDL oxidation in the human body and develop strategies to prevent and reduce atherosclerosis.

Thesis Committee:

Marc D. Donohue, Professor of Chemical Engineering

Aranovich Gregory, Principal Research Scientist of Chemical Engineering

Acknowledgements

I would like to greatly thank Professor Donohue for being my research advisor and for all of his guidance. I learned to model and apply computational & mathematical methods to solve complex problems from Professor Donohue's teaching and mentoring. His support has always pushed me to strive in his lab.

I would also like to thank Principal Research Scientist Aranovich Gregory for being on my thesis committee. Not only did his feedback help me understand my own research better, he kept me focused on the task at hand. In addition, I would like to thank my co-worker, Tiankai Zhang, and senior student Minxue Jia, who have helped me for my research work a lot.

Lastly, I would like to thank my friends and family, especially my parents, who have supported and helped me throughout this process and deserve all of the credit.

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Chapter 1. Methods

We propose a simplified model for the transfer of triglycerides and cholesterol via lipoproteins and the oxidation of fatty acids in the body. Since LDL is the product of very low-density lipoprotein (VLDL) dilapidation, the essential steps are modeling the metabolism of VLDL. In order to accomplish this, our model first describes the basic metabolism of chylomicron (CM), chylomicron remnant (CMR), the circulation of triglyceride (TG), cholesterol (CH), cholesterol ester (CE), fatty acids (FFA) and their reactions in liver, muscle and adipose tissues. Next step, the modeling of VLDL synthesis is included. Eventually, this model is formulated to follow the generation of oxidation LDL.

1.1 Modeling of the cholesterol and triglyceride pool in liver

A mass balance is considered with the chylomicron input from diet. Chylomicron carried triglyceride cholesterol and different types of fatty acids which we will discuss later. Chylomicrons becomes chylomicron remnants by giving up triglycerides which are hydrolyzed by lipoprotein lipase in adipose plasma compartment and muscle plasma compartment. The hydrolysis production, triglycerides and fatty acids, go through the whole body by plasma circulation and go to different organs by diffusion. The cholesterol in die, all transport to liver by the endocytosed of chylomicron remnant. Other important cholesterol sources in the liver includes HDL and LDL. HDL is assembled by ApoA1 and cholesterol as well as phospholipids which are extracted from tissues, and eventually HDL is taken up by SR-B1, transport the cholesterols back to liver. The LDL receptor, responses for the endocytose of LDL, is present in the liver, muscle, adipose and other peripheral tissue, but the liver is the principal organ in clearing LDL via the LDL receptor. If LDL particles are oxidized, the affinity between LDL and LDL receptor will dramatically decrease. The lipoprotein metabolism is shown in the Figure 1.

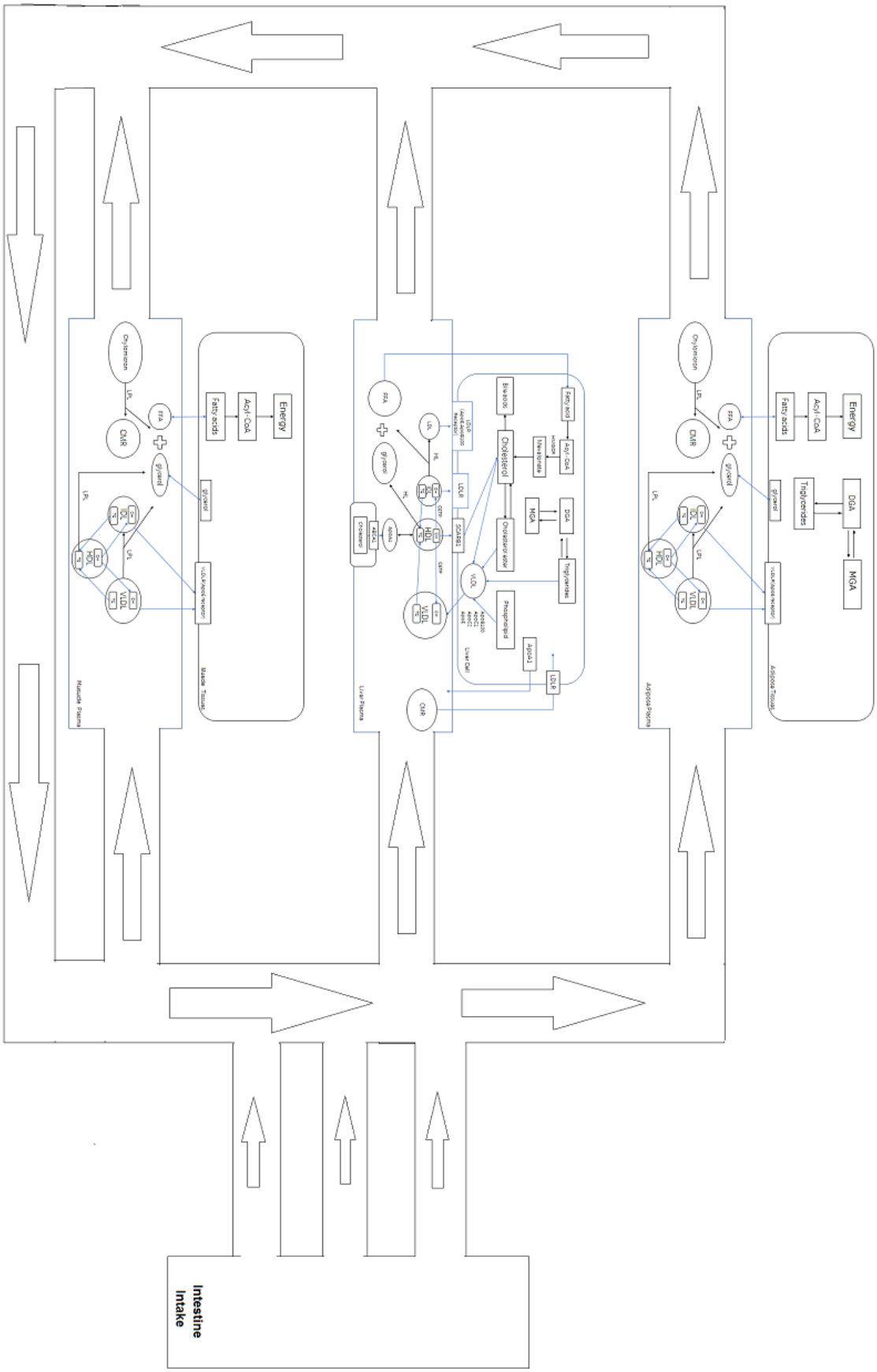

Figure 1. Lipoprotein Metabolism

1.2 The modeling of VLDL formation.

VLDL is a triglyceride-enriched particle produced in the liver. The triglyceride content of VLDL is broken down into free fatty acids and glycerol rapidly by LPL. Eventually, VLDL is convert to IDL and LDL when the triglyceride content below a certain level. The production of VLDL can be regulated by multiple factors. In our model, if is assumed that the ApoB100 production rate is constant. Since one ApoB100 will assemble one VLDL micelles, the number of newly synthesized VLDL particles is unaffected by liver cholesterol and triglyceride amount. However, the composition of VLDL will be affected by the liver cholesterol and triglyceride concentration change. Moreover, the fatty acid composition is accounted for in the model, because with different ratios of saturate fatty acids, mono-unsaturated fatty acids, and poly-unsaturated fatty acids, the triglyceride transport rate from liver to VLDL is different.[1] Therefore, with different dietary oil we use, we will get different composition of VLDL, which directly affects the oxidation LDL generation of oxidation LDL.

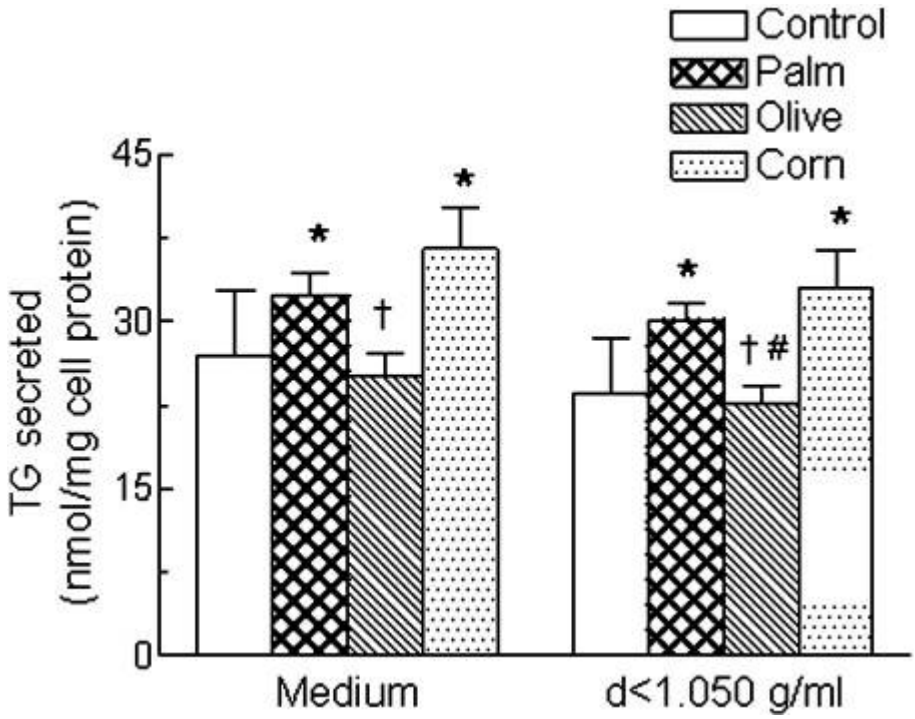

Figure 2. the amount of TG secreted in VLDL with different oil[1]

1.3 The modeling of oxidation LDL formation.

With lipoprotein micelle circulation with plasma throughout the body, they will contact with oxidant such as free radicals. The component of VLDL, mainly consist of cholesterol and triglyceride, sometimes has unsaturated fatty acids tail. Since the unsaturated fatty acids have the high susceptibility to oxidation by reactive oxygen species or free radicals, the polyunsaturated fatty acid easily become fatty acid radical by attaching free radical. Then fatty acid radical will react with molecular oxygen and produce peroxyl fatty acid radical. Finally, peroxyl fatty acid radical reacts with other unsaturated fatty acid to produce oxidized phospholipids or reactive lipid aldehydes such as malondialdehyde(MDA) which are able to modify the structure of apolipoproteins such as ApoB100. LDL with modified apolipoproteins cannot be recognized by LDL receptors and cleared by the lipoprotein circulating system so eventually these LDL with modified apolipoproteins will only be taken up by macrophage through scavenger receptors in intima and this promotes the development of atherosclerosis.

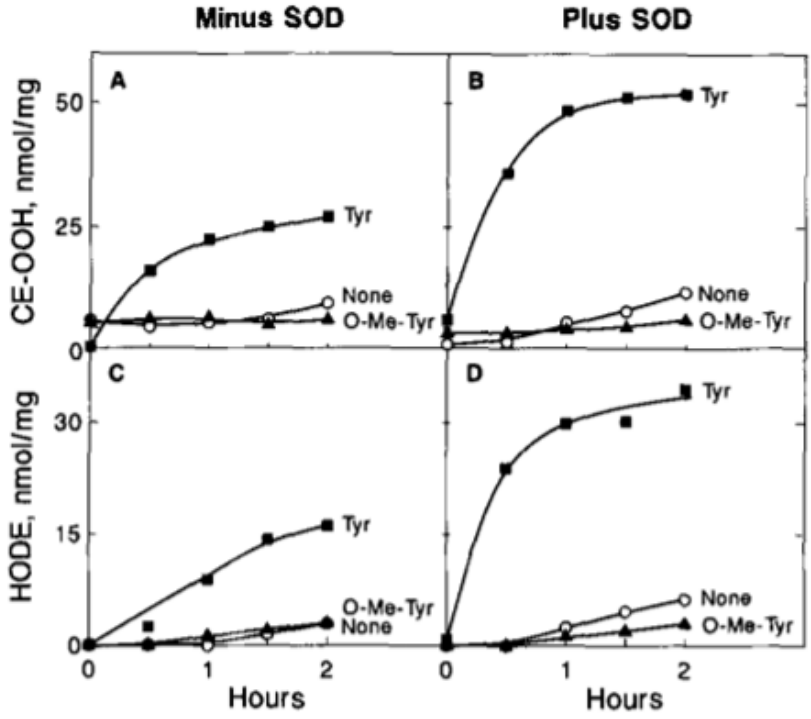

Figure 3. the oxidation reaction rate of unsaturated TG and CE [2]

Chapter 2. Result

The first results show the concentration change lipids from the ODE model. The dietary lipid input is given through infusion of chylomicron, whose amount depends on basal metabolism rate. The model predicts the total lipid concentration change in liver, muscle and adipose tissues. We assume that different fatty acids don't change the transportation rate, therefore other parts of the model remain unchanged for different dietary oils. In adipose and muscle, the triglyceride amount continuous increase due to the accumulation rate exceed the consumption rate. Because adipose tissue can use fatty acids produce triglycerides, these triglycerides accumulate more faster in adipose tissues.

Because the input and output terms of cholesterol in muscle cells are both quite low, the concentration of cholesterol in muscle almost remains the constant.

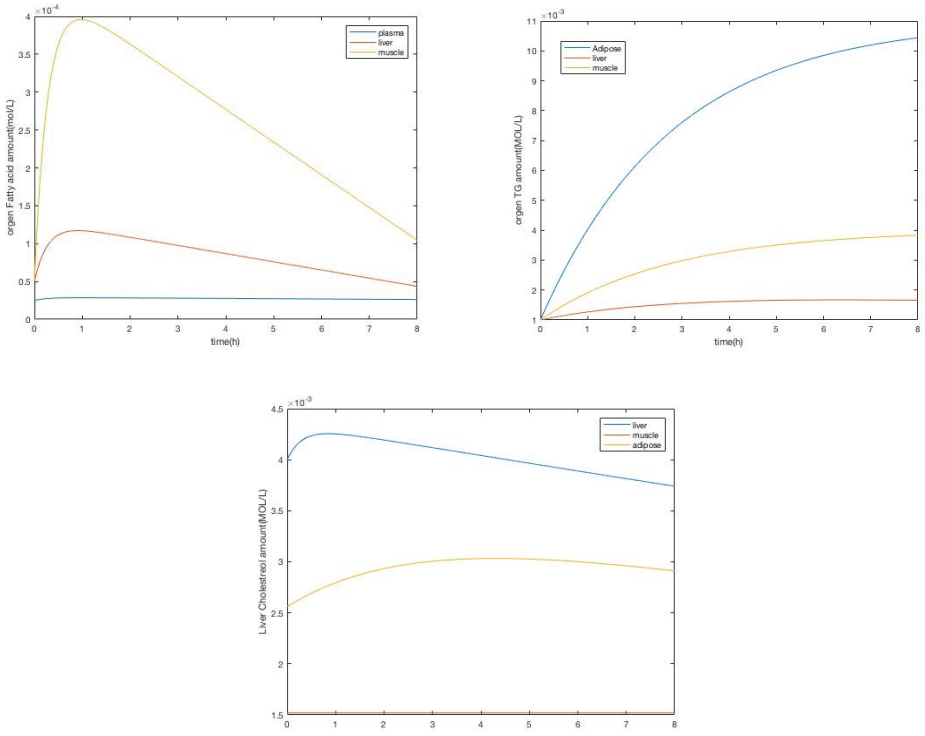

Figure 4. Lipid concentrations in different organs

The second part of the model is the VLDL composition of triglycerides.

Generally, the greater polyunsaturated fatty acid ratio is, the more triglycerides will accumulate in VLDL[1]. Therefore, VLDL generated from a diet containing corn oil will have the most triglyceride in it. For palm oil and olive oil, the total triglycerides amount in VLDL is almost the same, due to their similar polyunsaturated fatty acids ratio. When it comes to unsaturated triglycerides, at the initial step, all fatty acids are saturated. With time passing, unsaturated fatty acids accumulate in liver, bind to the glycerol proportionally. Palm oil has the least VLDL unsaturated triglycerides amount since palm oil has the greatest ratio of saturate fatty acids among all three oils.

	Saturated fatty acids (%)	Monounsaturated fatty acids (%)	Omega-3 fatty acids (%)	Omega-6 fatty acids (%)
Palm oil	49.3	37	0.2	9.1
Olive oil	13.8	73	0.7	9.8
Corn oil	12.9	27.6	1	58

Table 1. Different dietary oil composition

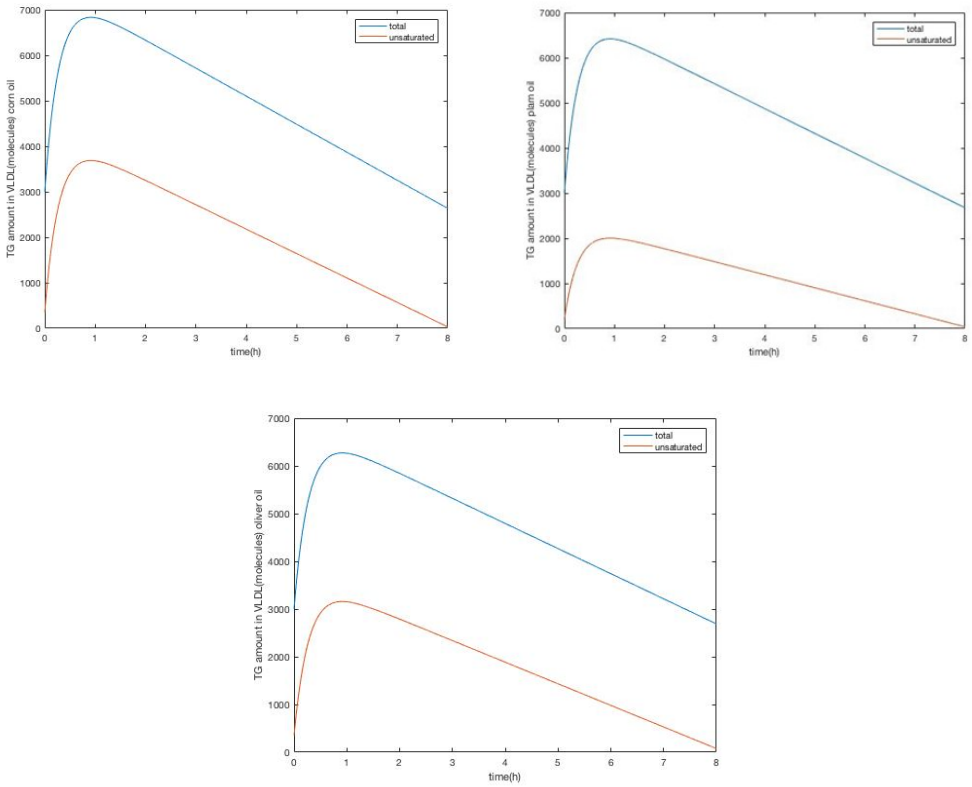

Figure 5. VLDL triglycerides composition of different dietary oil

Figure. 6 shows how cholesterol ester accumulate in VLDL. The total concentration is same for all three oils, but they have different unsaturated cholesterol concentrations. Based on the unsaturated triglycerides and cholesterol amount in VLDL, we calculate the total double bond number in each single VLDL. For most omega-3 fatty acids, there are 3 double bonds, and 2 double bonds for most omega-6 fatty acids. Although the total amount of unsaturated lipid is similar between corn oil and olive oil, the double bond number in corn oil VLDL is nearly double then the olive oil VLDL. We assume that, even if two double bonds lie on the same molecular, they can individually react to free radical, and the oxidation degree of lipoprotein depends on the ratio of oxidization double bonds, not on the oxidation molecule.

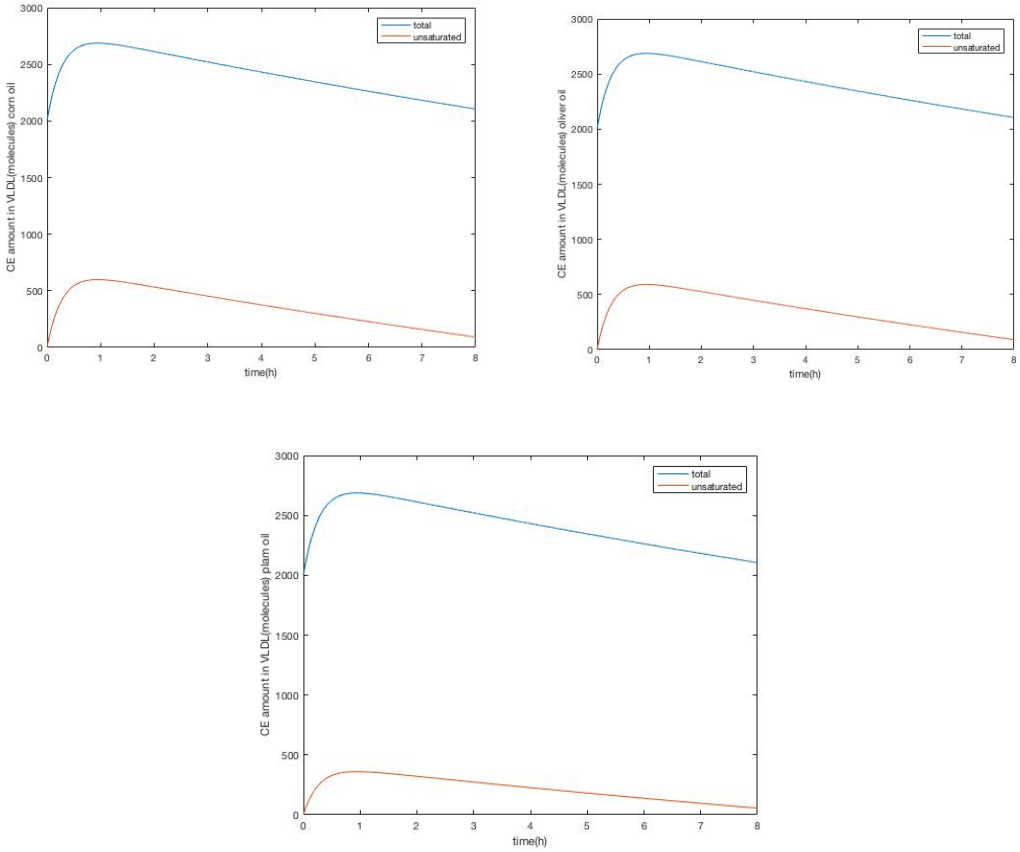

Figure 6. VLDL cholesterol ester composition of different dietary oil

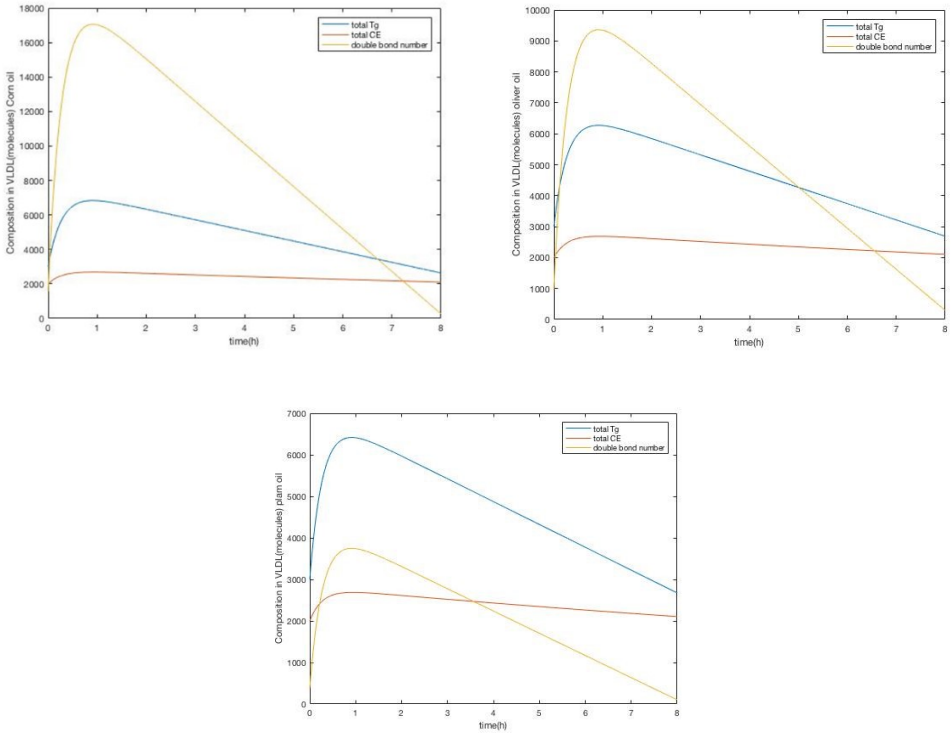

Figure 7. VLDL composition and double bonds number

To calculate the possibility of VLDL converting to oxidization LDL, we must simulate the VLDL metabolism. There are four reactions involved in VLDL metabolism in our model: unsaturated triglyceride oxidation, unsaturated cholesterol ester oxidation, triglycerides hydrolyzation and cholesterol transformation between HDL and VLDL via CETP. Because the hydrolyzation rate is nearly 20 times faster then oxidation rate, the concentration of triglycerides decreases dramatically while oxidation double number slowly increases. The number of oxidization double bonds depends on the composition of dietary fatty acids and the triglyceride amount in VLDL. Oxidation VLDL double bond number nearly doubled in high triglycerides VLDL compared to low triglycerides VLDL after 8 hours. The cholesterol concentration is regulated by CETP. At the first couple of hours, the concentration increases due to the cholesterol transport from HDL to VLDL. However, with the cholesterol amount decrease in HDL, CETP will bring some cholesterol back to HDL.

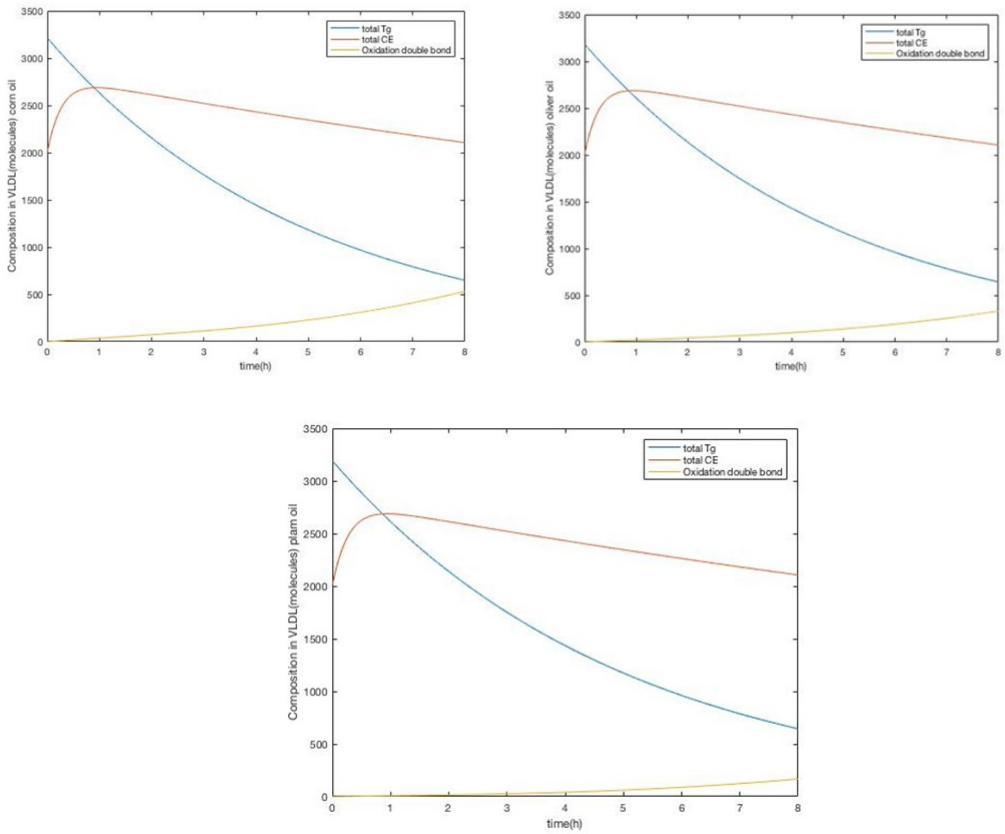

Figure 8. metabolism for low triglycerides VLDL

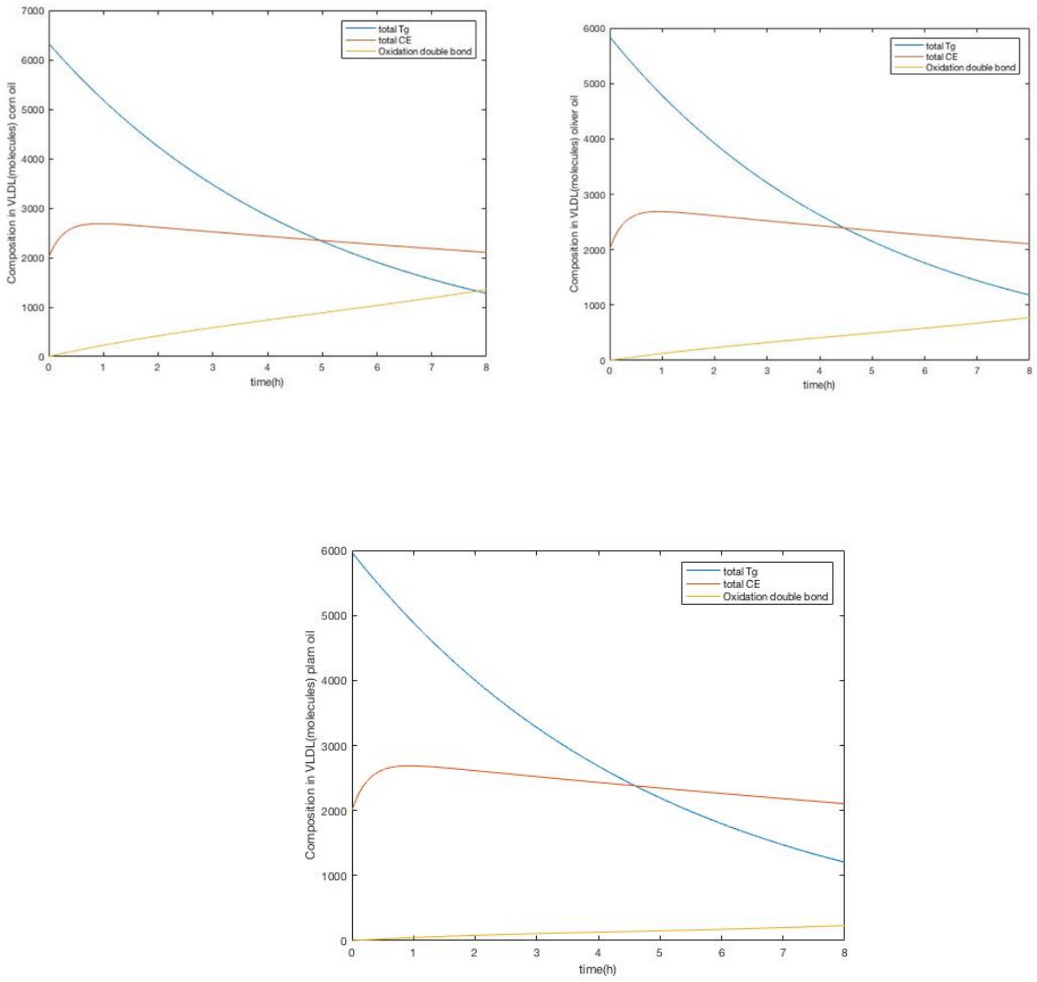

Figure 9. metabolism for high triglycerides VLDL

Chapter 3. Discussion and limitation

We propose an assumption about formation of oxidized cholesterol and triglyceride in LDL and build an ODE model demonstrates the lipoprotein and lipid metabolism in a numerical way. The excessive lipid intake would result in the increased generation rates of VLDL and LDL. The elevated VLDL and LDL level promote CETP and higher formation of oxidized LDL production and heightened risk of atherosclerosis.

This model elucidates the fatty acid transport within the human body. The fatty acid composition in the daily diet can lead to different composition of the liver fatty acid pool, which results in a significant change in the number of oxidation double bonds in LDL. We demonstrate that, compare to the corn oil dietary, the palm oil diet reduces approximately 60% oxidized double bonds in low triglycerides micelles and 80% in high triglycerides fatty acids. The reduction of oxidized double bonds due to palm oil reduces the triglycerides amount in VLDL. It is not a surprise that the palm oil dietary produces the least oxidation LDL.

However, lower number of triglycerides in VLDL means generally liver must produce more VLDL to meet the triglycerides and cholesterol needs of other tissue cells. Although in our model, the number of new synthesized VLDL remains constants, in reality the situation will be much more complicates. Therefore, although in single VLDL, the lower double bond number reduces the possibility that the micelles convert to oxidized LDL, more VLDL number will generate more oxidation LDL. We believe that this is the greatest limitation of this model. Including the ApoB100 production change will be a possible way to improve our model.

Moreover, we only show the metabolism of VLDL in a short period of time. From what we learned, the triglycerides hydrolyze rate can be much faster than the oxidation rate of double bonds. Which means that the oxidation double bonds contribute to triglyceride oxidation can be small, since before being oxidized, most unsaturated fatty acids already released in plasma by triglycerides hydrolyzation. Therefore, unsaturated cholesterol ester may contribute most of oxidized double bonds in LDL. That might explain why high intake of cholesterol will increase the

risk of cardinal vascular disease.

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Reference

[1] López-Soldado I, Avella M, Botham K M. Differential influence of different dietary fatty acids on very low-density lipoprotein secretion when delivered to hepatocytes in chylomicron remnants[J]. Metabolism, 2009, 58(2): 186-195.

[2] Wieland E, Parthasarathy S, Steinberg D. Peroxidase-dependent metal-independent oxidation of low density lipoprotein in vitro: a model for in vivo oxidation? [J]. Proceedings of the National Academy of Sciences, 1993, 90(13): 5929-5933.

Appendix. Differential Equation and chemical reaction use in model.

Appendix I. Liver Plasma equations:

1. Unsaturated triglyceride oxidation

Unsaturated triglyceride + [o] ⟶ oxidized triglyceride

2. Unsaturated cholesterol ester oxidation

Unsaturated cholesterol ester + [o] ⟶ oxidized cholesterol ester

3. Saturated triglyceride hydrolysis

Saturated triglyceride ⟶ 3 Saturated Fatty acid + Glycerol

4. Unsaturated triglyceride hydrolysis

Unsaturated triglyceride ⟶ 3 Unsaturated Fatty acid + Glycerol

1.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{o}] * [\boldsymbol{uTG}]$$

2.

$$-\frac{\mathrm{d[uCHE]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{o}] * [\boldsymbol{uCHE}]$$

3.

$$-\frac{\mathrm{d[sTG]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{sTG}]$$

4.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{uTG}]$$

Appendix II. Liver equations:

5. Saturated cholesterol ester production

Cholesterol + Saturated Fatty acid ⟶ Saturated cholesterol ester

6. Unsaturated cholesterol ester production

Cholesterol + Unsaturated Fatty acid ⟶ Unsaturated cholesterol ester

7. MGA/DGA/TG balance

Fatty acid + Glycerol ⟷ Monoglyceride

Fatty acid + Monoglyceride ⟷ Diglyceride

Fatty acid + Diglyceride ⟷ Triglyceride

8. VLDL assembly

Triglyceride + Cholesterol ester + phospholipid + ApoB100 ⟶ VLDL

9. Beta-oxidation

Saturated Fatty acid ⟶ nAcetyl-CoA

Unsaturated Fatty acid ⟶ nAcetyl-CoA

10. Citric acid cycle

Acetyl-CoA ⟶ ATP

11. Mevalonate pathway

3Acetyl-CoA ⟶ Mevalonic acid

12. CETP transfer process

2Saturated triglyceride + Cholesterol ester loading CETP ⟶ Saturated triglyceride loading CETP + 2Cholesterol ester

2Unsaturatedtriglyceride+Cholesterol ester loading CETP ⟶ Unsaturated triglyceride loading CETP + 2Cholesterol ester

2Cholesterol ester + Saturated triglyceride loading CETP ⟶ Cholesterol ester loading CETP + 2Saturated triglyceride

2Cholesterol ester + Unsaturated triglyceride loading CETP ⟶ Cholesterol ester loading CETP + 2Unsaturated triglyceride

13. HDL formation

ApoA1 + Cholesterol ⟶ HDL

5.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH] * [sFFA]$$

6.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH] * [uFFA]$$

7.

$$-\frac{\mathrm{d[FFA]}}{\mathrm{dt}} = k * [FFA] * [GLY] - k' * [MGA]$$

$$-\frac{\mathrm{d[MGA]}}{\mathrm{dt}} = k * [FFA] * [MGA] - k' * [DGA]$$

$$-\frac{\mathrm{d[DGA]}}{\mathrm{dt}} = k * [FFA] * [DGA] - k' * [TG]$$

8.

$$-\frac{\mathrm{d[CE]}}{\mathrm{dt}} = k * [CE]$$

$$-\frac{\mathrm{d[PL]}}{\mathrm{dt}} = k * [PL]$$

$$-\frac{\mathrm{d[TG]}}{\mathrm{dt}} = k * [TG]$$

$$-\frac{\mathrm{d[ApoB100]}}{\mathrm{dt}} = k * [ApoB100]$$

9.

$$-\frac{\mathrm{d[sFFA]}}{\mathrm{dt}} = k * [sFFA]$$

$$-\frac{\mathrm{d[uFFA]}}{\mathrm{dt}} = k * [uFFA]$$

10.

$$-\frac{\mathrm{d[AcetylCoA]}}{\mathrm{dt}} = k * [\mathrm{AcetylCoA}]$$

11.

$$-\frac{\mathrm{d[AcetylCoA]}}{\mathrm{dt}} = k * [\mathrm{AcetylCoA}]^3$$

12.

$$-\frac{\mathrm{d[sTG]}}{\mathrm{dt}} = k * [CCETP] * [sTG]^2$$

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = k * [CCETP] * [uTG]^2$$

$$-\frac{\mathrm{d[CE]}}{\mathrm{dt}} = k * [sTGCETP] * [CE]^2$$

$$-\frac{\mathrm{d[CE]}}{\mathrm{dt}} = k * [uTGCETP] * [CE]^2$$

13.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH]$$

Appendix III. Adipose Tissue Plasma equations

1. Unsaturated triglyceride oxidation

Unsaturated triglyceride + [o] ⟶ oxidized triglyceride

2. Unsaturated cholesterol ester oxidation

Unsaturated cholesterol ester + [o] ⟶ oxidized cholesterol ester

3. Saturated triglyceride hydrolysis

Saturated triglyceride ⟶ 3 Saturated Fatty acid + Glycerol

4. Unsaturated triglyceride hydrolysis

Unsaturated triglyceride ⟶ 3 Unsaturated Fatty acid + Glycerol

1.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = \boldsymbol{k} * [o] * [\boldsymbol{uTG}]$$

2.

$$-\frac{\mathrm{d[uCHE]}}{\mathrm{dt}} = \boldsymbol{k} * [o] * [\boldsymbol{uCHE}]$$

3.

$$-\frac{\mathrm{d[sTG]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{sTG}]$$

4.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = \boldsymbol{k} * [\boldsymbol{uTG}]$$

Appendix IV. Adipose Tissue equations

5. Saturated cholesterol ester production

Cholesterol + Saturated Fatty acid ⟶ Saturated cholesterol ester

6. Unsaturated cholesterol ester production

Cholesterol + Unsaturated Fatty acid ⟶ Unsaturated cholesterol ester

7. MGA/DGA/TG balance

Fatty acid + Glycerol ⟷ Monoglyceride

Fatty acid + Monoglyceride ⟷ Diglyceride

Fatty acid + Diglyceride ⟷ Triglyceride

8. Beta-oxidation

Saturated Fatty acid ⟶ nAcetyl-CoA

Unsaturated Fatty acid ⟶ nAcetyl-CoA

9. Citric acid cycle

Acetyl-CoA ⟶ ATP

10. CETP transfer process

2Saturated triglyceride + Cholesterol ester loading CETP ⟶ Saturated triglyceride loading CETP + 2Cholesterol ester

2Unsaturatedtriglyceride+Cholesterol ester loading CETP ⟶ Unsaturated triglyceride loading CETP + 2Cholesterol ester

2Cholesterol ester + Saturated triglyceride loading CETP ⟶ Cholesterol ester loading CETP + 2Saturated triglyceride

2Cholesterol ester + Unsaturated triglyceride loading CETP ⟶ Cholesterol ester loading CETP + 2Unsaturated triglyceride

11. HDL formation

ApoA1 + Cholesterol ⟶ HDL

5.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH] * [sFFA]$$

6.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH] * [uFFA]$$

7.

$$-\frac{\mathrm{d[FFA]}}{\mathrm{dt}} = k * [FFA] * [GLY] - k' * [MGA]$$

$$-\frac{\mathrm{d[MGA]}}{\mathrm{dt}} = k * [FFA] * [MGA] - k' * [DGA]$$

$$-\frac{\mathrm{d[DGA]}}{\mathrm{dt}} = k * [FFA] * [DGA] - k' * [TG]$$

8.

$$-\frac{\mathrm{d[sFFA]}}{\mathrm{dt}} = k * [sFFA]$$

$$-\frac{\mathrm{d[uFFA]}}{\mathrm{dt}} = k * [uFFA]$$

9.

$$-\frac{\mathrm{d[AcetylCoA]}}{\mathrm{dt}} = k * [\mathrm{AcetylCoA}]$$

10.

$$-\frac{\mathrm{d[sTG]}}{\mathrm{dt}} = k * [CCETP] * [sTG]^2$$

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = k * [CCETP] * [uTG]^2$$

$$-\frac{\mathrm{d[CE]}}{\mathrm{dt}} = k * [sTGCETP] * [CE]^2$$

$$-\frac{\mathrm{d[CE]}}{\mathrm{dt}} = k * [uTGCETP] * [CE]^2$$

11.

$$-\frac{\mathrm{d[CH]}}{\mathrm{dt}} = k * [CH]$$

Appendix V. Muscle Plasma equations

1. Unsaturated triglyceride oxidation

Unsaturated triglyceride + [o] ⟶ oxidized triglyceride

2. Unsaturated cholesterol ester oxidation

Unsaturated cholesterol ester + [o] ⟶ oxidized cholesterol ester

3. Saturated triglyceride hydrolysis

Saturated triglyceride ⟶ 3 Saturated Fatty acid + Glycerol

4. Unsaturated triglyceride hydrolysis

Unsaturated triglyceride ⟶ 3 Unsaturated Fatty acid + Glycerol

1.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = k * [o] * [uTG]$$

2.

$$-\frac{\mathrm{d[uCHE]}}{\mathrm{dt}} = k * [o] * [uCHE]$$

3.

$$-\frac{\mathrm{d[sTG]}}{\mathrm{dt}} = k * [sTG]$$

4.

$$-\frac{\mathrm{d[uTG]}}{\mathrm{dt}} = k * [uTG]$$

Appendix VI. Muscle equations

5. Saturated cholesterol ester production

Cholesterol + Saturated Fatty acid → Saturated cholesterol ester

6. Unsaturated cholesterol ester production

Cholesterol + Unsaturated Fatty acid → Unsaturated cholesterol ester

7. Beta-oxidation

Saturated Fatty acid → nAcetyl-CoA

Unsaturated Fatty acid → nAcetyl-CoA

8. Citric acid cycle

Acetyl-CoA → ATP

9.CETP transfer process

2Saturated triglyceride + Cholesterol ester loading CETP → Saturated triglyceride loading CETP + 2Cholesterol ester

2Unsaturatedtriglyceride+Cholesterol ester loading CETP → Unsaturated triglyceride loading CETP + 2Cholesterol ester

2Cholesterol ester + Saturated triglyceride loading CETP → Cholesterol ester loading CETP + 2Saturated triglyceride

2Cholesterol ester + Unsaturated triglyceride loading CETP → Cholesterol ester loading CETP + 2Unsaturated triglyceride

10.HDL formation

ApoA1 + Cholesterol → HDL

5.

$$-\frac{\mathbf{d[CH]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{CH}] * [\boldsymbol{sFFA}]$$

6.

$$-\frac{\mathbf{d[CH]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{CH}] * [\boldsymbol{uFFA}]$$

7.

$$-\frac{\mathbf{d[sFFA]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{sFFA}]$$

$$-\frac{\mathbf{d[uFFA]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{uFFA}]$$

8.

$$-\frac{\mathbf{d[AcetylCoA]}}{\mathbf{dt}} = \boldsymbol{k} * [\mathbf{AcetylCoA}]$$

9.

$$-\frac{\mathbf{d[sTG]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{CCETP}] * [\boldsymbol{sTG}]^2$$

$$-\frac{\mathbf{d[uTG]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{CCETP}] * [\boldsymbol{uTG}]^2$$

$$-\frac{\mathbf{d[CE]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{sTGCETP}] * [\boldsymbol{CE}]^2$$

$$-\frac{\mathbf{d[CE]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{uTGCETP}] * [\boldsymbol{CE}]^2$$

10.

$$-\frac{\mathbf{d[CH]}}{\mathbf{dt}} = \boldsymbol{k} * [\boldsymbol{CH}]$$

Resume

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EDUCATION

Johns Hopkins University, Baltimore, MD
Whiting School of Engineering
Sept 2017-present
Master of Chemical & Biomolecular Engineering graduation: 2019
Graduate-level Coursework: Project in Design: Pharmacokinetics, Advanced Topics in Pharmacokinetics and Pharmacodynamics, Transport Phenomena in Practice, Advanced Chemical Reaction Engineering in Practice

Nanjing University, Nanjing, China
Bachelor of Science in Chemistry Sept 2013- June 2017
Intensive Instruction in Science, taking courses in Computer Science Department
Related Coursework: Basics of Programming(C++), Modeling and Statistical Analysis of Data for Chemical Engineers Data Structures, Linear Algebra, Probability and Statistics, Calculus

TECHNICAL SKILLS & KNOWLEDGE

Programming: C++, MATLAB, Python
Data Analysis, modeling & visualization: Scipy, NumPy, Pandas, Scikit-learn, Tidyverse, dplyr, etc.
Others: Machine Learning, Algorithms and Realization, Algorithms, Data Structures, SQL, Excel, Microsoft Office, Linux etc.

ACADEMIC PROJECTS

- **Pharmacodynamics and Metabolism of Fats and Sugars in Humans (Research Project)**
- Johns Hopkins University, Baltimore, MD Feb 2018
  - Try to developing a comprehensive pharmacodynamics model of the glucose and lipid metabolism and the connections between the two in order to elucidate the connections between the various aspects of metabolic syndrome
  - Implemented all jobs by MATLAB Python
  - Building algorithm to predict the lipid oxidation intermediate concentration change

- **Pharmacokinetics modelling for melanoma drugs (Course Project)**
- Johns Hopkins University, Baltimore, MD Sep 2017- Dec 2017
  - Use multi compartment model to model melanoma drugs absorb.
  - Use model to compare IV, subcutaneous fat, intra muscular injection or infusion, find the best drug intake method.

- Pharmacodynamics modelling for type-2 diabetes (Course Project)
- Johns Hopkins University, Baltimore, MD Sep 2018-Dec-2018
  - Building model to predict the blood sugars concentrations change for healthy and type-2 diabetes patient.
  - Modelling different type of diabetes drug to elucidate their Pharmacodynamics effect.